



## General

### Guideline Title

ACR Appropriateness Criteria® infertility.

### Bibliographic Source(s)

Wall DJ, Bhosale PR, Harisinghani MG, Harris RD, Khati NJ, Mitchell DG, Nyberg DA, Pandharipande PV, Pannu HK, Shipp TD, Siegel CL, Simpson L, Wong-You-Cheong JJ, Zelop CM, Javitt MC, Glanc P, Expert Panel on Women's Imaging. ACR Appropriateness Criteria® infertility [online publication]. Reston (VA): American College of Radiology (ACR); 2014. 12 p. [100 references]

### Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Recommendations

### Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Infertility

Variant 1: Clinical features or history of polycystic ovary syndrome.

Radiologic Procedure	Rating	Comments	RRL*
US pelvis transvaginal	9		O
US pelvis transabdominal	7		O
MRI pelvis without and with contrast	6		O
MRI pelvis without contrast	5		O
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: History or clinical suspicion of endometriosis.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	8		O
US pelvis transvaginal	8		O
Hysterosalpingography	7	Consider this procedure in the clinical setting of infertility.	<input type="text"/> <input type="text"/>
US pelvis transabdominal	7		O
MRI pelvis without contrast	7		O
US pelvis endorectal	6	Consider this procedure if there is concern of deep endometriosis or recurrent endometriosis.	O
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Suspicion of tubal occlusion, pelvic inflammatory disease or history of pelvic surgery.

Radiologic Procedure	Rating	Comments	RRL*
Hysterosalpingography	9		<input type="text"/> <input type="text"/>
US pelvis transvaginal	8	This procedure may be performed with HyCoSy.	O
US pelvis transabdominal	7		O
MRI pelvis without and with contrast	7		O
MRI pelvis without contrast	6		O
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Recurrent pregnancy loss.

Radiologic Procedure	Rating	Comments	RRL*
US saline infusion sonohysterography	8	This procedure may be performed with HyCoSy. Recommend addition of 3-D imaging to assess for Müllerian duct anomalies and Asherman syndrome.	O
MRI pelvis without and with contrast	8		O
MRI pelvis without contrast	8		O
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

US pelvis transabdominal	6		O
Hysterosalpingography	5		<input type="text"/> <input type="text"/>
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: Galactorrhea present on physical examination.

Radiologic Procedure	Rating	Comments	RRL*
MRI head without and with contrast	8	Consider multiplanar thin sellar imaging.	O
MRI head without contrast	7	Consider multiplanar thin sellar imaging.	O
CT head without and with contrast	5	This procedure is indicated if MRI is not available or is contraindicated.	<input type="text"/> <input type="text"/> <input type="text"/>
CT head with contrast	4	This procedure is indicated if MRI is not available or is contraindicated.	<input type="text"/> <input type="text"/> <input type="text"/>
CT head without contrast	4	This procedure is indicated if MRI is not available or is contraindicated.	<input type="text"/> <input type="text"/> <input type="text"/>
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

### Summary of Literature Review

#### Introduction/Background

Infertility is defined as the inability to achieve a successful pregnancy after 12 or more months of regular unprotected intercourse. About 15.5% of women experience infertility; however, in many women this may be temporary as time to pregnancy data show a decrease in infertility at 24 months compared to 12 months. Although infertility investigation usually begins at this point, it may commence sooner in women older than age 35, or in those with a known condition or medical history predisposing to infertility.

The most common causes of infertility in couples are ovulatory failure (21%), tubal damage (14%), and male factor (26%). Infertility is unexplained in 28% of couples. Female-specific causes of infertility include ovulatory disorders, most notably polycystic ovarian disease, deterioration of oocyte quality with increasing maternal age, history of salpingitis such as that caused by chlamydia infection, endometriosis, and uterine cavity abnormalities.

Infertility investigation begins with a thorough history and physical examination. A detailed history including previous pregnancies and infertility treatments, menstrual history, frequency of intercourse, medication and toxin exposures, and factors predisposing to pelvic adhesions (surgery, endometriosis, pelvic inflammatory disease) is necessary. Physical examination is not limited to the pelvis, but also includes palpation of the thyroid, a thorough breast examination to look for secretions, and assessing for signs of androgen excess. Following clinical and laboratory evaluation, imaging is often utilized in the assessment of infertility.

#### Overview of Imaging Modalities

Hysterosalpingography (HSG) is used to evaluate tubal patency and the uterine cavity contour and to a lesser degree the cervical canal morphology. Conditions that may be detected with HSG include congenital malformations, polyps, submucosal leiomyomas, synechiae, adenomyosis, tubal occlusion, salpingitis isthmica nodosa, hydrosalpinx, and peritubal adhesions. HSG is regarded as safe; however, the procedure exposes patients to ionizing radiation and potentially allergenic contrast media. HSG is contraindicated in patients with active pelvic inflammatory disease or pregnancy. There is a relative contraindication in patients with a previous allergic reaction to iodinated contrast agents. Antibiotic administration or prophylactic use of antibiotics is at the discretion of the referring physician if there is a prior history of pelvic infection or if hydrosalpinx is noted at the time of the study. Laparoscopy with chromopertubation is widely accepted as the gold standard for evaluating tubal patency.

Transvaginal ultrasound (TVS) is useful in evaluating the ovaries, uterus, fallopian tubes, and adnexa. It also is readily available, relatively low in cost, and without ionizing radiation. During infertility evaluation, TVS can be used to monitor follicle development, perform antral follicle counts, assess for polycystic ovaries, and look for evidence of endometriosis. The endometrium and uterus are well assessed by routine TVS. Contrast sonohysterography or saline-infusion sonohysterography (SIS) provides an assessment of the uterine cavity. The addition of hysterosalpingocontrast sonography (HyCoSy) provides a comparable assessment of tubal patency and uterine cavity to HSG. Antibiotic administration or prophylactic use of antibiotics is at the discretion of the referring physician if there is a prior history of pelvic infection or if hydrosalpinx is noted at the time of the study.

Although the endometrium can be assessed by TVS, SIS is particularly useful in assessing potential causes of infertility including intrauterine adhesions, endometrial polyps, and leiomyomas. Recently, three-dimensional ultrasound (3-D US) has become useful in the evaluation of female infertility in its ability to improve upon detection of lesions within the uterine cavity and improve classification of congenital uterine anomalies. 3-D US has been widely used in conjunction with SIS.

HyCoSy involves instilling echogenic contrast into the uterus with real-time US to observe the material distending the uterine cavity, filling the fallopian tubes, and spilling out over the adjacent ovary. This technique does not involve exposure to ionizing radiation nor potential allergic reaction to iodine based contrast agents. However, US contrast agents are not currently approved for use in the United States. In the interim some providers utilize agitated saline to assess tubal patency, the accuracy of which is less validated.

Magnetic resonance imaging (MRI) of the pelvis has excellent soft-tissue contrast and multiplanar imaging capability without ionizing radiation. MRI provides accurate assessment of uterine contour anomalies potentially contributing to infertility such as congenital uterine anomalies, adenomyosis, and leiomyomas. Endometriosis, another potential cause of female infertility, can also be evaluated with MRI. Intracranial MRI is also the most useful imaging examination in the evaluation of pituitary microadenomas.

#### Discussion of Imaging Modalities by Variant

##### *Variant 1: Clinical Features or History of Polycystic Ovary Syndrome*

Polycystic ovary syndrome (PCOS) is the leading cause of anovulatory infertility. PCOS is not only associated with infertility, but also with an increased risk of dysfunctional bleeding, obesity, type 2 diabetes mellitus, dyslipidemia, hypertension, and cardiovascular disease. In addition, a meta-analysis showed women with PCOS are 3 times more likely to develop endometrial cancer; however, one recent retrospective study of 963 premenopausal women with PCOS showed no difference in the likelihood of developing endometrial carcinoma between women with and without PCOS.

In 2009, the Androgen Excess and PCOS Society proposed the following criteria for diagnosing PCOS: hyperandrogenism and ovarian dysfunction with the exclusion of other androgen excess or related disorders. Hyperandrogenism typically presents as hirsutism, the presence of terminal hairs on the face and/or body in a female in a male-type pattern. Ovarian dysfunction can include ovulatory dysfunction or polycystic ovaries, as defined by ovarian volume greater than 10 cc or 12 or more follicles between 2 and 9 mm in diameter with no dominant follicle on TVS. Increased echogenicity of the ovarian stroma has been reported as the most sensitive and specific sign of polycystic ovaries; however, this is a subjective finding. MRI can demonstrate decreased signal intensity of the central stroma with small peripheral cysts on T2-weighted images; however, these findings are not specific for PCOS.

##### *Variant 2: History or Clinical Suspicion of Endometriosis*

Endometriosis affects at least one-third of women with infertility and up to 10% of reproductive-aged women. Although endometriosis is associated with infertility, the mechanism is unclear. HSG to assess tubal patency and the uterine cavity has been proposed as part of an infertility workup in women with endometriosis. However, in one study 21% of women undergoing infertility evaluation were found to have endometriosis at surgery despite a normal HSG.

Although imaging is useful in characterizing some features of endometriosis, small endometrial implants are not well detected. Thus laparoscopy

remains the standard for both diagnosis and staging of endometriosis. Transrectal US was shown to be 97% sensitive and 96% specific for the detection of rectovaginal endometriosis. The same study demonstrated 80% sensitivity and 97% specificity in diagnosing uterosacral ligament implants. This technique is limited to a small anatomic area and is not widely used. Although not sensitive for the detection of tiny endometrial implants, TVS can demonstrate macroscopic endometriomas that are often bilateral. On US, an endometrioma typically appears as an adnexal or ovarian mass with diffuse, low-level internal echoes. This appearance is 95% sensitive and 81% specific for the diagnosis of an endometrioma. The presence of echogenic foci in the wall (hemosiderin deposits) or multilocularity increases the likelihood that a mass with this appearance is an endometrioma. MRI has been shown to be 82% to 90% sensitive and 91% to 98% specific for the diagnosis of endometriomas.

The typical MRI features of an endometrioma are high signal on T1 with low signal on T2-weighted images (T2 shading) from intracellular methemoglobin, crosslinking of proteins, and iron. Peritoneal implants can be detected with MRI, although the sensitivity is only 61% and specificity is 87%. Adhesions can also be present in endometriosis. If the uterus is fixed in retroversion, then adhesions may be suspected. A recent study retrospectively evaluated the usefulness in assessing MRI findings of uterine retroflexion, retrouterine fibrous mass, displacement of intraperitoneal fluid, elevation of the posterior vaginal fornix, and adherence/angulation of bowel loops to the posterior surface of the uterus in the diagnosis of posterior cul-de-sac obliteration from endometriosis. This study found uterine retroflexion was only 24.4% sensitive in the diagnosis of posterior cul-de-sac obliteration. Adding the presence of a retroflexed uterus in approximately 20% of patients without endometriosis, this finding is not a reliable predictor of endometriosis. The study did find that a T2 hypointense and T1 isointense or hypointense mass between the uterus and rectosigmoid junction as well as displacement of intraperitoneal free fluid from the posterior cul-de-sac were reliable predictors of posterior cul-de-sac obliteration by endometriosis. Adherence to or angulation of bowel loops toward the posterior surface of the uterus was 83.7% sensitive but more difficult to detect for less experienced readers. These findings may have been enhanced in this study due to the administration of vaginal and rectal sterile US gel, as well as intravenous (IV) glucagon. Another study similarly identified serosal uterine fibrotic plaques as having the best accuracy for posterior cul-de-sac obliteration but did not assess displacement of free pelvic fluid.

#### *Variant 3: Suspicion of Tubal Occlusion, Pelvic Inflammatory Disease, or History of Pelvic Surgery*

Women with a history of pelvic infection or surgery may develop intrauterine synechiae, fallopian tube abnormalities including occlusion, and peritubal adhesions. HSG allows detection of tubal patency, tubal size, tubal irregularity, and peritubal disease. It can also detect intrauterine synechiae, which typically present as irregular endometrial filling defects. Tubal flushing during HSG has also been shown to increase pregnancy rates up to 38% compared to pregnancy rate of up to 21% in women being investigated for infertility who did not undergo HSG, but the pregnancy rate was highest in women who underwent HSG with oil-soluble contrast. Unlike performance of HSG with water-soluble contrast agents, the use of oil-based contrast material for HSG carries the increased risk of oil emboli if there is myometrial intravasation.

Hydrosalpinx may occur in the setting of distal tubal occlusion, most commonly due to pelvic inflammatory disease. The finding of hydrosalpinx has implications for patients who may undergo in-vitro fertilization. TVS has been shown to be 86% sensitive in detecting hydrosalpinx. Apart from detection of hydrosalpinges, TVS has not been shown to be effective in documenting tubal patency. MRI is also useful in the detection of hydrosalpinges and is superior to TVS in the assessment of pelvic inflammatory disease (95% sensitive and 89% specific compared to 81% sensitive and 78% specific).

Although HSG has been regarded as the imaging study of choice in assessing tubal patency, it was only 65% sensitive and 85% specific for diagnosing tubal patency when compared to laparoscopy with chromopertubation. Magnetic resonance HSG is an additional technique that can demonstrate tubal patency and may be useful in women in whom both MRI and HSG need to be performed, but it is felt the catheterization technique will need to be improved as it cannot be adequately performed using a conventional MRI scanner. HyCoSy has also been compared to HSG and laparoscopy with chromopertubation. One meta-analysis found 83% concordance between HyCoSy and HSG as well as between HyCoSy and laparoscopy with chromopertubation in detecting tubal pathology. HyCoSy is felt to be comparable to HSG for tubal investigation. Although HyCoSy offers the ability to visualize the uterus, ovaries, and fallopian tubes in one exam, the lack of approved US contrast agents in the United States has limited its applicability.

#### *Variant 4: Recurrent Pregnancy Loss*

Recurrent pregnancy loss affects approximately 5% of couples. Evaluation for a cause of recurrent pregnancy loss should be performed after the third consecutive early miscarriage. Numerous causes or contributing factors to recurrent pregnancy loss have been identified including immunologic, chromosomal, endocrine disorders, uterine anomalies, clotting disorders, infections, and chemical exposures. Potential anatomic causes include Müllerian anomalies, synechiae, and leiomyomas. Up to 10% of women suffering recurrent pregnancy loss have a congenital Müllerian anomaly.

In 1988, the American Society of Reproductive Medicine (previously known as the American Fertility Society) modified and updated the classification system for Müllerian duct anomalies (MDA). This remains the classification system in use today. Septate uterus is the most common anomaly and results from partial or complete failure of resorption of the uterovaginal septum. It has been theorized that recurrent fetal loss results

from abnormal endometrium and/or abnormal vascularity on the septum. Resection of the septum (hysteroscopic metroplasty) has been shown to improve spontaneous abortion rates in these patients. Bicornuate uterus is generally not corrected surgically. Due to the differences in treatment between septate and bicornuate uteri, it is essential to evaluate the external uterine contour for differentiation. On both TVS and MRI, a fundal cleft >1 cm can be used to diagnose a bicornuate uterus and differentiate it from a septate uterus (fundal cleft <1 cm). A fundal indentation <5mm above the interostial line can also be used for identification of a bicornuate uterus. In contrast to a septate uterus, an arcuate uterus demonstrates slight indentation of the fundal endometrium secondary to near complete resorption of the uterovaginal septum. This may be considered a normal variant and may not affect reproduction.

Incomplete fusion of the uterovaginal horns at the uterine fundus causes a bicornuate uterus. Although affected women typically have little difficulty conceiving, spontaneous abortion and preterm delivery rates are higher than in the general population. About 25% of patients with bicornuate uterus have an upper vaginal septum. Surgery is typically not indicated as length of gestation often increases with subsequent pregnancies. There is also a higher incidence of cervical incompetence.

Didelphys uteri occur when the Müllerian ducts completely fail to fuse. Usually there are 2 cervical canals. There is no communication between the uterine cavities. Women with this anomaly may have dysmenorrhea, endometriosis, and pelvic adhesions. Transverse vaginal septa may cause hematometrocolpos secondary to obstruction at the level of the vagina. However, it is much more common to find a nonobstructing longitudinal vaginal septum seen in up to 75% of cases.

When one of the Müllerian ducts fails to develop, a unicornuate uterus occurs. There is an unexplained predominance of right sided unicornuate uterus, (i.e., impaired development on the left). There is often a left rudimentary horn which may or may not communicate with the right horn and may have functioning endometrium. Hematometra and ectopic pregnancy are risks in the rudimentary horn, prompting resection. Approximately 40% of women with a unicornuate uterus have a unilateral renal anomaly.

A meta-analysis of 9 studies investigating reproductive outcomes in women with congenital uterine anomalies grouped women into 3 different categories: arcuate uteri, canalization defections, and unification defects. Those with arcuate uteri were found to have an increased rate of second-trimester pregnancy loss and fetal malpresentation. Those with canalization defects such as septate and subseptate uteri were found to have difficulty conceiving, first-trimester pregnancy loss, preterm birth, and fetal malpresentation. Those with unification defects such as unicornuate, bicornuate, and didelphys uteri suffered increased incidence of preterm birth and fetal malpresentation.

In 24 cases of surgically proven MDA, MRI was 100% accurate, 2-dimensional (2-D) TVS was 92% accurate, and hysterosalpingogram was only 16.7% accurate. Although HSG can visualize the uterine cavity, it cannot provide information about the external uterine contour, preventing accurate distinction between a septate and a bicornuate uterus. 3-D US has been shown to have similar accuracy to MRI, with the benefit of being less expensive. However, this technique is currently not widely available.

MDA are also associated with renal anomalies. Approximately 30% of women with MDA have renal agenesis, more frequently those with didelphys uteri and unicornuate uterus. Screening for renal anomalies should therefore be considered in women with MDA.

Intrauterine adhesions have been reported in up to 39% of women with recurrent pregnancy loss, though it is unclear how often these adhesions cause the loss of pregnancy. Though hysteroscopy is the gold standard for visualizing intrauterine adhesions, imaging examinations may have a role in the diagnosis as well. A study of 54 women with suspected Asherman syndrome discovered 3-D US was 100% sensitive, and HSG was 66.7% sensitive in grading intrauterine adhesions compared to hysteroscopy. Another study of only 19 women discovered HSG and sonohysterography were both 100% sensitive, and conventional TVS was only 52% sensitive for detecting intrauterine adhesions compared to hysteroscopy. Additional studies have shown HSG to be 75% to 81% sensitive and 80% specific compared to hysteroscopy in diagnosing intrauterine adhesions. Although MRI may be useful in detecting intrauterine adhesions, no large studies comparing its efficacy to hysteroscopy have been performed.

An additional possible anatomic cause for recurrent pregnancy loss is fibroids. It is difficult to confirm a direct causal relationship between pregnancy loss and fibroids, especially given the high prevalence of fibroids in the fertile population. Incidence of fibroids in women of reproductive age is estimated to reach 10%, and 8.2% of 966 women in a study of women suffering from recurrent pregnancy loss were found to have fibroids. In a study of 140 women who underwent hysteroscopy during infertility evaluation, all had an HSG and 93 also underwent SIS. Compared to hysteroscopy, HSG was 52.6% accurate and SIS was 75% accurate in detecting fibroids. In another study of 133 women undergoing infertility evaluation who underwent both hysteroscopy and TVS, TVS detected submucosal fibroids in 10 of the 11 patients diagnosed with submucosal fibroids at hysteroscopy, yielding a sensitivity of 91% and specificity of 100%. A systematic review of studies involving women with abnormal uterine bleeding demonstrated hysteroscopy and SIS to be better than TVS in detecting submucosal fibroids. When comparing diagnostic modalities to hysterectomy for the detection of intracavitary abnormalities, MRI, SIS, and hysteroscopy were equally effective and superior to TVS.

*Variant 5: Galactorrhea Present on Physical Examination*

Galactorrhea is nonlactational milk production. It has many causes including pregnancy, hypothalamic and pituitary disorders, hypothyroidism, renal insufficiency, medication-induced, and hyperestrogenemia. Patients with galactorrhea and an elevated prolactin level and no other identifiable cause should undergo imaging evaluation for a sellar or suprasellar mass, including prolactinomas, macroadenomas, lymphocytic hypophysitis, granulomas, Rathke cleft cysts, and other suprasellar masses.

Adenomas are the most common sellar mass. These can be either functional or nonfunctional with prolactinomas being the most common functional tumor. Hyperprolactinemia caused by these masses can cause infertility. Although computed tomography (CT) can be useful in assessing erosion of the sellar floor or destruction of the sphenoid sinus by sellar masses, MRI is the most widely used and accepted method for sellar and suprasellar imaging.

No Other Signs or Symptoms

Following appropriate clinical workup, a suspected cause of infertility will not be identified in some women. Given that some etiologies of infertility are clinically silent, appropriate imaging studies should still be performed at the discretion of the infertility specialist to evaluate tubal patency and the uterine cavity.

Summary of Recommendations

- Selection of appropriate imaging examinations in patients undergoing infertility workup will depend on clinical history and physical examination findings.
- TVS is the preferred modality to assess for radiologic features of PCOS.
- In women who have a history or clinical suspicion of endometriosis, both MRI and pelvic US can provide valuable information. HSG is also appropriate in these women when undergoing infertility workup.
- HSG is the preferred method of imaging women with a suspicion of tubal occlusion.
- Women suffering from recurrent pregnancy loss will benefit from SIS, MRI, or transvaginal 3-D US.
- MRI of the head to assess the pituitary gland is appropriate in women with galactorrhea and laboratory studies suggestive of a pituitary adenoma.

Abbreviations

- 3-D, three-dimensional
- CT, computed tomography
- HyCoSy, hysterosalpingocontrast sonography
- MRI, magnetic resonance imaging
- US ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
<div></div>	<0.1 mSv	<0.03 mSv
<div></div> <div></div>	0.1-1 mSv	0.03-0.3 mSv
<div></div> <div></div> <div></div>	1-10 mSv	0.3-3 mSv
<div></div> <div></div> <div></div> <div></div>	10-30 mSv	3-10 mSv
<div></div> <div></div> <div></div> <div></div> <div></div>	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

# Scope

## Disease/Condition(s)

Infertility

## Guideline Category

Diagnosis

Evaluation

## Clinical Specialty

Obstetrics and Gynecology

Radiology

## Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

## Guideline Objective(s)

To evaluate the appropriateness of various imaging modalities for the evaluation of women with infertility

## Target Population

Women undergoing infertility investigation

## Interventions and Practices Considered

1. Ultrasound (US)
  - Pelvis, transvaginal
  - Pelvis, transabdominal
  - Pelvis, endorectal
  - Saline-infusion sonohysterography (SIS)
2. Magnetic resonance imaging (MRI)
  - Pelvis, without and with contrast
  - Pelvis, without contrast
  - Head, without and with contrast
  - Head, without contrast
3. Computed tomography (CT), head
  - Without and with contrast



- With contrast
- Without contrast

#### 4. Hysterosalpingography (HSG)

## Major Outcomes Considered

- Utility of radiologic examinations in differential diagnosis of infertility
- Sensitivity and specificity of radiologic examinations in diagnosis
- Incidence and prevalence of infertility

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

#### Literature Search Summary

A literature search was conducted in February 2013 to identify evidence for the *ACR Appropriateness Criteria® Infertility* topic. Using the search strategy described in the literature search companion (see the "Availability of Companion Documents" field), 111 articles were found. Three articles were used in the topic. One hundred and eight articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, or the results were unclear, misinterpreted, or biased.

The author added 97 citations from bibliographies, Web sites, or books that were not found in the literature search.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

### Number of Source Documents

Three articles were used in the topic. The author added 97 citations from bibliographies, Web sites, or books that were not found in the literature search.

### Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

#### Study Quality Category Definitions

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - There are important study design limitations.

Category 4 - The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:

- a. The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description).
- b. The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence.
- c. The study is an expert opinion or consensus document.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development documents (see the "Availability of Companion Documents" field).

## Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

## Description of Methods Used to Formulate the Recommendations

### Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness. When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate", is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the second

rating round, the recommendation is "May be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized and economical process. For additional information on the ratings process see the [Rating Round Information](#)  document on the ACR Web site.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the [ACR Web site](#)  (see also the "Availability of Companion Documents" field).

## Rating Scheme for the Strength of the Recommendations

Not applicable

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Internal Peer Review

## Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

#### Summary of Evidence

Of the 100 references cited in the *ACR Appropriateness Criteria® Infertility* document, 2 are categorized as therapeutic references including 1 well-designed study and 1 good quality study. Additionally, 98 references are categorized as diagnostic references including 1 well-designed study, 9 good quality studies, and 15 quality studies that may have design limitations. There are 73 references that may not be useful as primary evidence.

While there are references that report on studies with design limitations, 12 well-designed or good quality studies provide good evidence.

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate selection of radiologic imaging procedures for the evaluation of women with infertility

### Potential Harms

- Hysterosalpingography (HSG) exposes patients to ionizing radiation and potentially allergenic contrast media.
- The use of oil-based contrast material for HSG carries the increased risk of oil emboli if there is myometrial intravasation.

- Ultrasound (US) contrast agents are not currently approved for use in the United States. In the interim some providers utilize agitated saline to assess tubal patency, the accuracy of which is less validated.

### Relative Radiation Level

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

## Contraindications

### Contraindications

Hysterosalpingography (HSG) is contraindicated in patients with active pelvic inflammatory disease or pregnancy. There is a relative contraindication in patients with a previous allergic reaction to iodinated contrast agents.

## Qualifying Statements

### Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

## IOM Domain

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

Wall DJ, Bhosale PR, Harisinghani MG, Harris RD, Khati NJ, Mitchell DG, Nyberg DA, Pandharipande PV, Pannu HK, Shipp TD, Siegel CL, Simpson L, Wong-You-Cheong JJ, Zelop CM, Javitt MC, Glanc P, Expert Panel on Women's Imaging. ACR Appropriateness Criteria® infertility [online publication]. Reston (VA): American College of Radiology (ACR); 2014. 12 p. [100 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2014

## Guideline Developer(s)

American College of Radiology - Medical Specialty Society

## Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

## Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Women's Imaging

## Composition of Group That Authored the Guideline

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## Financial Disclosures/Conflicts of Interest

Not stated

## Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Electronic copies: Available from the [American College of Radiology \(ACR\) Web site](#) .

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

## Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Feb. 3 p. Electronic copies: Available from the [American College of Radiology \(ACR\) Web site](#) .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Electronic copies: Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Evidence table development – therapeutic studies. Reston (VA): American College of Radiology; 2013 Nov. 4 p. Electronic copies: Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2015 Feb. 3 p. Electronic copies: Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2015 Feb. 2 p. Electronic copies: Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria® infertility. Evidence table. Reston (VA): American College of Radiology; 2014. 40 p. Electronic copies: Available from the [ACR Web site](#) .
- ACR Appropriateness Criteria® infertility. Literature search. Reston (VA): American College of Radiology; 2014. 1 p. Electronic copies: Available from the [ACR Web site](#) .

## Patient Resources

None available

## NGC Status

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